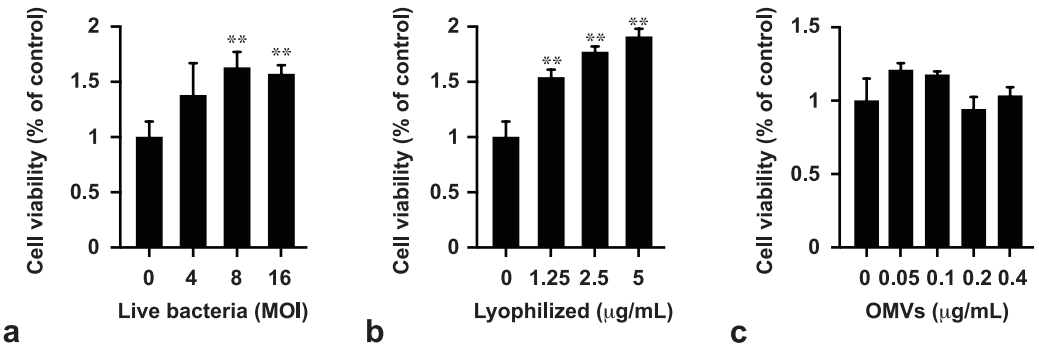**Supplementary Figure 2**